

CLAIMS

1. A method for predicting a drug transport capability of a mammalian cell comprising the steps of:

5 collecting a sample from a mammal,
 determining a polymorphism of the nucleotide sequence of *ABCG2* gene or a polymorphism of the amino acid sequence of *ABCG2* polypeptide.

2. The method of claim 1, wherein said *ABCG2* gene comprises a DNA
10 consisting of the nucleotide sequence of SEQ ID NO:1, and said polymorphism of the nucleotide sequence is one or more of single nucleotide polymorphisms at positions selected from the group consisting of 34, 376 and 421 of SEQ ID NO:1.

3. The method of claim 2, wherein said single nucleotide polymorphism is
15 selected from the group consisting of G34A, C376T and C421A.

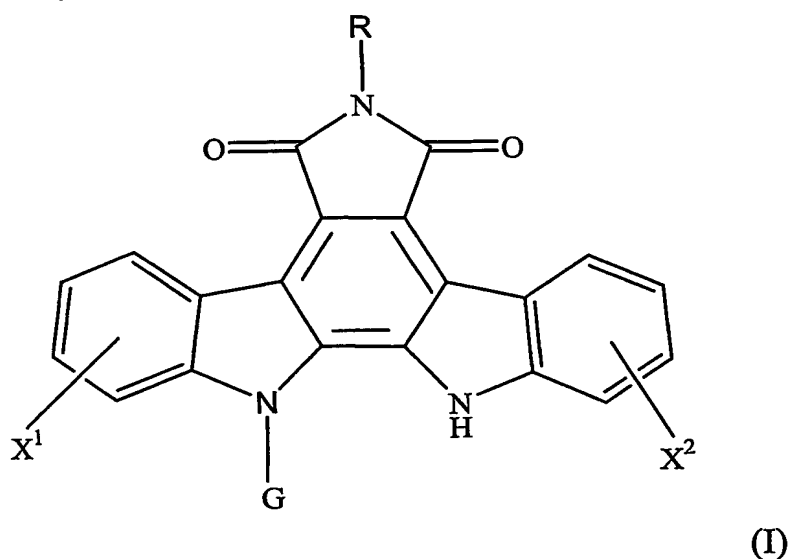
4. The method of claim 2, wherein said polymorphism of the nucleotide
20 sequence is determined by any one of methods selected from the group consisting of a direct sequencing method, TaqMan method, invader method, mass spectrometry, RCA method and DNA chip method.

5. The method of claim 1, wherein said *ABCG2* polypeptide comprises an
amino acid sequence of SEQ ID NO:2, and said polymorphism of the amino acid
sequence is one or more of amino acid polymorphisms at positions selected
25 from the group consisting of 12, 126, and 141 of SEQ ID NO:2.

6. The method of claim 5, wherein said amino acid polymorphism is an
amino acid substitution of Val12Met or Gln141Lys, or a deletion of the amino
acid sequence downstream from the position 126 of SEQ ID NO:2.

7. The method of claim 5, wherein said polymorphism of the amino acid sequence is determined by any one of methods selected from the group consisting of mass spectrometry, two-dimensional electrophoresis method, and protein chip method.

8. The method of any one of claims 1 to 7, wherein said drug is a compound represented by the following general formula (I):



wherein X¹ and X² each independently represent a hydrogen atom, halogen atom or hydroxyl group,

R represents a hydrogen atom, amino, formylamino, or lower alkylamino which may be substituted with any one selected from the group consisting of one to three hydroxyl group(s), a pyridyl group optionally having substituent(s), and thienyl group optionally having substituent(s), and

G represents a pentose group or hexose group or derivative thereof which may be substituted with an amino group.

9. A polynucleotide having a single nucleotide polymorphism(s) at one or more position(s) selected from the group consisting of 34, 376 and 421 of SEQ

ID NO:1, said polynucleotide comprising any one of the positions of said single nucleotide polymorphisms and consisting of at least 10 contiguous nucleotides of SEQ ID NO:1, or a complementary polynucleotide thereto.

5 10. The polynucleotide of claim 9, wherein said single nucleotide polymorphism is selected from the group consisting of G34A, C376T, C421A and single nucleotide polymorphisms complementary thereto.

10 11. A polynucleotide having one or more of the nucleotide polymorphisms in the polynucleotide sequence of SEQ ID NO:1, said polymorphism selected from the group consisting of nucleotide polymorphisms by which the translated amino acid at position 12 is methionine, one at position 126 is stop codon, and one at position 141 is lysine, and consisting of at least 10 contiguous nucleotides including one or more of nucleotides located at the site of said nucleotide
15 polymorphisms, or a complementary polynucleotide thereto.

12. A pair of PCR primers which specifically hybridize to *ABCG2* gene, and amplify a DNA fragment of a portion of said gene, wherein the amplified DNA fragment comprises a nucleotide(s) at position 34, 376 or 421 of SEQ ID NO:1
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13. The pair of PCR primers of claim 12, said pair of PCR primers selected from the group of:

SEQ ID NO:5 and SEQ ID NO:6; SEQ ID NO:9 and SEQ ID NO:10; and
SEQ ID NO:11 and SEQ ID NO:12.

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14. A polynucleotide which specifically hybridizes to *ABCG2* gene, and which is capable of detecting a polymorphism(s) of *ABCG2* gene at position 34, 376 or 421 of SEQ ID NO:1.

15. The polynucleotide of claim 14, which is capable of using in any one of methods selected from the group consisting of a direct sequencing method, TaqMan method, invader method, mass spectrometry, RCA method and DNA chip method.

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16. A polypeptide having polymorphic mutation(s) to ABCG2 protein defined in the following (a) or (b), said polypeptide is a polymorphic mutant wherein one or both of amino acids at positions 12 and 141 of SEQ ID NO:2 are substituted with other amino acid(s), a polypeptide fragment comprising said substituted amino acid and at least 10 contiguous amino acid residues of said polymorphic mutant, or a polypeptide wherein the amino acid sequence downstream from the position 126 of SEQ ID NO:2 is deleted:

(a) a human ABCG2 polypeptide consisting of an amino acid sequence of SEQ ID No: 2,

15 (b) an isopolypeptide of (a) consisting of an amino acid sequence of SEQ ID NO:2, wherein one or several amino acids except for the amino acids at positions 12, 126 and 141, are deleted, substituted or added, and having a drug transport capability.

20 17. An antibody which specifically binds to the mutant ABCG2 polypeptide of claim 16.

18. A transformed cell which expresses an polypeptide having polymorphic mutation(s) to ABCG2 protein defined in the following (a) or (b), said polymorphic mutation(s) being one or both of amino acid substitutions Val12Met and Gln141Lys of the amino acid sequence of SEQ ID NO:2:

25 (a) a human ABCG2 polypeptide consisting of an amino acid sequence of SEQ ID NO:2,

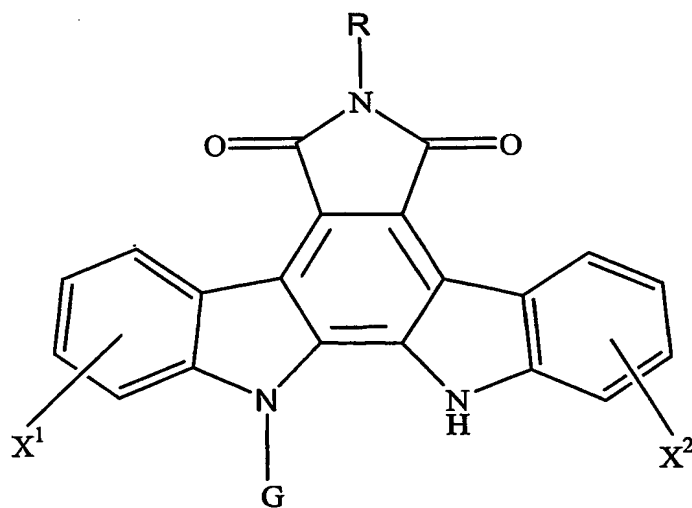
(b) an isopolypeptide of (a) consisting of an amino acid sequence of

SEQ ID NO:2, wherein one or several amino acids except for the amino acids at positions 12, 126 and 141, are deleted, substituted or added, and having a drug transport capability.

5 19. A method for measuring a drug transport capability using the transformed cell of claim 18.

20. A method for diagnosing a drug sensitivity comprising the steps of:
analyzing a biological sample from a subject, and determining the presence or
10 absence of a polynucleotide of any one of claims 9 to 11, or a polypeptide of claim 16.

21. The method of claim 20, wherein the subject having said polynucleotide and/or said polypeptide is suggested to be sensitive to the compound
15 represented by the following general formula (I):



(I)

wherein X¹ and X² each independently represent a hydrogen atom, halogen atom or hydroxyl group,

R represents a hydrogen atom, amino, formylamino, or lower alkylamino
20 which may be substituted with any one selected from the group consisting of one

to three hydroxyl group(s), a pyridyl group optionally having substituent(s), and thienyl group optionally having substituent(s), and

G represents a pentose group or hexose group or derivative thereof which may be substituted with an amino group.

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22. A kit for diagnosing a drug sensitivity comprising one or more of the following (a) to (f):

- (a) the polynucleotide of any one of claims 9 to 11,
- (b) the pair of primers of claim 12 or 13,
- 10 (c) the polynucleotide of claim 14 or 15,
- (d) the polypeptide of claim 16,
- (e) the antibody of claim 17, and
- (f) the transformed cell of claim 18.

15 23. A computer system for analyzing data of ABCG2 polymorphism, comprising:

- (a) an input/output device,
- (b) a memory containing the polymorphism data, and
- (c) a central processing unit.